REMARKS

Claims 2 – 4 are currently pending. In the Office Action, Claims 2 – 4 were rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of Hoorn et al. (US 6,835,853) (hereinafter, "Hoorn"). Claims 2 – 4 were also rejected under § 103(a) as allegedly obvious over Fujikura et al. (AT 397,960) (hereinafter, "Fujikura").

Each of the foregoing rejections is respectfully traversed and favorable reconsideration is requested in view of the above amendments and following remarks.

I. Cancellation of Withdrawn Claims.

As in initial matter, Claims 5 – 10, which were previously withdrawn from examination, have now been cancelled, without prejudice. While Claims 5 – 10 have been cancelled, Applicants expressly reserve the right to prosecute the subject matter of these claims in one or more divisional or other applications.

II. Prior Art Rejections.

The present claims are directed to a reaction mixture formed from the alkylation of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide with a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene. The reaction mixture is principally comprised of tamsulosin hydrochloride, but also includes at least some measurable amount of undesired, "overalkylated" side products or impurities.

The desired tamsulosin hydrochloride is formed when one molecule of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide reacts with one molecule of 1-(2-bromoethoxy)- 2-ethoxybenzene. The undesired "overalkylated"products, on the other hand, are believed to be formed when two or more molecules of 1-(2-bromoethoxy)-2-ethoxybenzene react and combine with a single molecule of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide.

The compounds 5-(2-(bis-(2-(2-ethoxyphenoxy)ethyl)amino)propyl)

-2- methoxybenzenesulphon-amide and N-(2-(2-ethoxyphenoxy)ethyl)-5-(2-(2-(2-ethoxyphenoxy)ethylamino)propyl)-2-methoxybenzenesulphonamide are two examples of these unwanted overalkylated products in the reaction mixture.

Production of tamsulosin hydrochloride by alkylation of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene is a particularly desirable synthesis route because a relatively small number of synthesis steps are required. However, it has been observed that these overalkylated products tend to be formed when tamsulosin hydrochloride is made by synthesis reactions using 1-(2-bromoethoxy)-2-ethoxybenzene, and conventional wisdom would counsel one to avoid of an excess of 1-(2-bromoethoxy)- 2-ethoxybenzene to reduce or eliminate production of these undesirable overalkylated products. However, Applicants have found the reverse to be true. Applicants have unexpectedly found that the measurable amount of overalkylated products is limited to less than 0.1% when a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene is used in the reaction in accordance with the Applicants' claimed invention.

It is important to appreciate that tamsulosin hydrochloride may also be made by synthesis routes which do not involve the alkylation of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene. In synthesis routes which avoid or do not use 1-(2-bromoethoxy)- 2-ethoxybenzene, the aforementioned overalkylated products are also avoided entirely. Such synthesis routes have the disadvantage, however, of requiring more synthesis steps than the alkylation of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene, and in some cases use of unfavorable solvents and other drawbacks.

In light of the above discussion, it is respectfully submitted that neither Hoorn nor Fujikura discloses or suggests a reaction mixture according to the claimed invention. Hoorn focuses on a method for resolution of a preexisting racemic tamsulosin composition into its optical isomers by fractional crystallization of diastereomeric sulfonate salts of tamsulosin. At column 14, lines 18 – 61 and in Example 2A, Hoorn mentions a process for the synthesis of

tamsulosin by alkylation of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene, but in neither case does Hoorn say anything about using a molar excess of the latter. As described above, Applicants do not claim to have invented synthesis of tamsulosin by reacting R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene. It was known to do this before their invention. So Hoorn merely confirms the known prior art. Furthermore, the discussion in Hoorn at column 14, lines 18 – 61, makes no mention of the stoichiometry at all. And in Example 2A, Hoorn actually teaches the use of an approximately 2 to 1 molar excess of R-5-(2-aminopropyl)-2-methoxybenzenesulphonamide over 1-(2-bromoethoxy)-2-ethoxybenzene. [1] So, if anything, Hoorn teaches against what Applicants' claim.

As for Fujikura, alkylation of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide with 1-(2-bromoethoxy)- 2-ethoxybenzene is mentioned only in Examples 3 and 4. As with Hoorn, neither example uses a molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene. In fact, Fujikura teaches the reverse. In Example 3, Fujikura, like Hoorn, teaches the use of an approximately 2 to 1 molar excess of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide over 1-(2-bromoethoxy)-2-eth-oxybenzene. In Example 4, Fujikura teaches the use of a 4 to 1 excess of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide (976 mg) over 1-(2-bromoethoxy)- 2-ethoxybenzene used (245 mg). Thus, Fujikura also teaches a stoichiometry concept which is the exact reverse of that claimed by Applicants, and, like Hoorn, actually goes against what Applicants claim.

Given these profound differences, it is evident that neither Hoorn nor Fujikura can be said to suggest a reaction mixture as called for in Claim 2 – wherein a reaction product mixture formed from the alkylation of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide with a

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[1]The molecular weight of R-5-(2-aminopropyl)- 2-methoxybenzenesulphonamide is 244. The molecular weight of 1-(2-bromoethoxy)- 2-ethoxybenzene is 245. Since the molecular weights of the two reactants are nearly the same, their molar ratios are approximately the same as their mass ratios.

molar excess of 1-(2-bromoethoxy)- 2-ethoxybenzene contains tamsulosin hydrochloride along with at least some measurable quantity of overalkylated products in an amount less than about 0.1%.

In light of the foregoing, the present amendment is believed to place the application in a condition for allowance and entry of the foregoing amendments and allowance of Claims 2 – 4 is respectfully solicited.

In the event that this response is not timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension, along with any other fees which may be due with respect to this response, may be charged to our Deposit Account No. 12-2355.

Respectfully submitted,

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